UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/359,260	07/22/99	CAMPBELL R	P3250

HM12/1220

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EXAMINER	
PRASTHOFER, T	
ART UNIT	**PAPER NUMBER**
1627	5

DATE MAILED: 12/20/00

Please find below and/or attached an Office communication concerning this application or pr ceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/359,260	CAMPBELL ET AL.	
	Examiner	Art Unit	
	Thomas W Prasthofer	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2000 and 23 October 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-127* is/are pending in the application.

4a) Of the above claim(s) *1-73 and 96-1276* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Detailed Office Action

Status of the Application

Receipt is acknowledged of election of species and drawings filed on 10/12/00 and 10/23/00 respectively. Claims 1-127 are pending in the application and the status of the claims is as follows:

Response to Election/Restriction Traversal

Applicant's election of yi = f(xij) as species of "function," molecular weight, total charge, and hydrophobicity as species of "whole molecule parameters," and enhancement of beta-toxin production as species of "activity" in Paper No. 3 are acknowledged.

Applicant's election with traverse of claims 74-95 and election of species in Paper No. 3 is acknowledged. Applicants are notified that the restriction between Groups I, IV, and VIII is withdrawn.

The traversal is on the ground(s) that the products of Group V are produced by, not used in the methods of Groups I, IV, and VIII. This is not found persuasive because, as stated in paper No. 2, the components of Group V can be used in a materially different process such as the preparation of dietary supplements for animals. The components of Group V are used in the methods of Groups I, IV, and VIII before they can identified by the methods of Groups I, IV, and VIII. The restriction is in compliance with MPEP 806.05 (h).

With respect to Groups I, IV, and VIII and Group VII, applicants argue that the independent claim of Group VII and the independent claims of Groups I, IV, and VIII recite the same basic steps and these steps define the core of the invention and differences in claim language between the groups such as "parameter" vs. "whole molecule parameter", "compound" vs. "peptide" and whether or not the method is performed in culture media do not create distinct inventions, but simply vary the scope of the same invention as claimed. This is found not persuasive because the invention of Groups I, IV, and VIII (now a single group) is drawn to the method of identifying a culture medium component whereas Group VII (elected) is drawn to a method of identifying peptides with a predicted indicia. These methods are distinct. If applicants **declare equivalency** between Groups I, IV, and VIII and Group VII, then the examiner will combine all of the Groups I, IV, VII, and VIII into a single group.

With respect to Group VI and Groups I, IV, and VIII, applicants argue that Group VI represents a subcombination of the combination claims of Groups I, IV, and VIII in that it recites the two basic steps of the invention which result in predicting the activity of a peptide. This is found not persuasive because the inventions of Groups I, IV, and VIII do not require the culture medium component to be a peptide and are therefor capable of being practiced without using the invention of Group VI. The invention of Group VI does not involve the use of culture media and can be practiced independently of Groups I, IV, and VIII. The restriction is in compliance with MPEP 806.05 (c).

With respect to Group III and Group II, applicants argue that it is not possible to create a library of candidate compounds (Group III) representing each of the plurality of groups of compound isomers by any other method (Group II) than representing each of the plurality of groups of compound isomers as such candidate compounds. This is found not persuasive

because, as stated in paper No. 2, the test compound library can be made by another materially different process such as screening a combinatorial library. The restriction is in compliance with MPEP 806.05 (f).

With respect to Group VI and Group VII, applicants argue that Group VI represents a subcombination of the combination claims of Group VII in that it recites the two basic steps of the invention which result in predicting the activity of a peptide. This is found not persuasive because the two methods use different steps and produce different outcomes. Group VI is a method of **predicting indicia** of a property of a peptide and includes a step involving **prediction** that is not present in Group VII while Group VII is a method **of identifying a peptide** with predicted indicia of an activity and includes an **identifying** step that is not present in Group VI. These methods are distinct. If applicants **declare equivalency** between Groups I, IV, and VIII and Group VII, then the examiner will combine all of the Groups I, IV, VII, and VIII into a single group.

Claims 1-15, 18-30, 41-54, 57, 58, 96-112, and 127 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected method of identifying a culture medium component, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Claims 31-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected method of defining a test compound library, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Claims 36-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected libraries of virtual molecules, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 2.

Claims 16, 17, 55, 56, and 113-118 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected culture media and culture media components, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Claims 59-73 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected method of predicting an indicia property of a peptide, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

Claims 119-122 and 123-126 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected apparatus and computer program for identifying culture media components, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 3.

35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and **useful** process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

1. **Claims 74-95 are rejected under 35 U.S.C. 101** because the claimed invention lacks patentable utility. Applicant's claimed method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement must satisfy 35 USC 101 and 112 (1) as defined by the statute and case law. In this regard, Applicant is directed to MPEP 2107; 2107.01 and 210.02 which provide guidelines for determining the criteria for satisfying utility and enablement.

The presently claimed invention is a method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement. In the abstract on page 72 of the specification, applicants assert the following utility:

"This method finds use in methods of drug discovery, identifying components of culture medium, and identifying and/or designing peptides with particular pharmacological or therapeutic activities."

Other utilities provided in the specification include identifying components and lead compounds, developing improved products for diagnostic applications, and providing an improved environment for cell research and drug discovery. These utilities are not specific for reasons described in the following paragraphs.

Initially it is noted that merely disclosing the ability to make a compound or compounds (e.g. a library) is in itself insufficient utility to satisfy either 35 USC 101 or 112, first paragraph as determined by the U.S. Supreme Court. . Eg. See *Brenner v. Manson,* 383 U.S. 519, 148 USPQ 689 (1966). The final step in claim 74 is "identifying a second test peptide library," indicating that the end result of the method is an identified library of peptides.

According to the text of 35 USC sec. 101, an invention must be "useful". Our reviewing courts have applied the labels, "specific utility" (or "practical utility") to refer to this aspect of the "useful invention" requirement of sec. 101. (Nelson v. Bowler, 626 F.2d 853, 206 USPQ 881, 883 (CCPA 1980)). In Nelson, the court characterized "specific utility" (or "practical utility") as "a shorthand way of attributing real-world value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." (Id. at 856.) With respect to the issue of pharmaceutical utility and **vague assertions** of biological activity applicant is further directed to *In re Kirk* , 376 F.2d 936, 941, 153 USPQ 48, 52 (CCPA 1967)) and *Cross v. Iizuka* , 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), wherein the Federal Circuit labeled applicant's assertion of "biological activity" without more specifics as a "nebulous" expression. Such statements, the court held, "convey little explicit indication regarding the utility of a compound" and do not satisfy either the utility and/or the enablement statutory requirements.

The claimed method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement is not supported by a specific asserted utility and does not, without further research and experimentation, provide an immediate benefit to the public. Rather, the claimed method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement is a means of identifying compounds that are merely candidates for culture media components or drug research. Any benefit to the public (to one of ordinary skill in the art) is speculative. There is no basis in the specification upon which to conclude that *any* of the peptides identified are, or will turn out to be, biologically active after testing.

A method of identifying a test peptide with a predicted indicia of an activity that satisfies a test requirement does not have a specific utility and no specific utility is disclosed in the specification. Identifying lead compounds is an invitation to experiment rather than a specific utility because test compounds can be leads for insecticides, food additives, glues, cosmetics, or treatments, cures, prophylactics, or diagnostics for any disease or condition. Applicant's asserted utility, e.g. for someone else (other than applicant) to *identify lead compounds and predict the structures of additional leads (e.g new compounds)* by using the presently claimed method clearly represents an invitation to experiment. *See Brenner v. Manson* cited above.

This is not to say that inventions that are to be used exclusively in a research setting (i.e., research tools) always lack a specific asserted utility. Indeed, many research tools such as telescopes, gas chromatographs, screening assays, and nucleotide sequencing techniques have a clear, specific and unquestionable utility. (See USPTO Utility Guidelines, page 12.)

However, inventions that have a specifically identified utility must be distinguished from those whose utility requires further research to identify or reasonably confirm. (Id.) Research tools (such as gas chromatographs, screening assays, etc.) are useful in the sense that they can be used in conjunction with other method steps to evaluate materials other than themselves or to arrive at some result.

The claimed method of identifying a peptide with predicted indicia of an activity that satisfies a test requirement is not a research tool in this sense. Rather, it is itself the subject of basic research, whose usefulness or lack thereof has yet to be established.

In the absence of an asserted specific utility, the "useful" requirement may be established by reference to a well established utility. A "well established utility" is a "specific utility" which is well known, immediately apparent and implied by the specification based on the disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The method of identifying a peptide with predicted indicia of an activity that satisfies a test requirement claimed is not supported by a well established utility, however, because the test requirement and therefor the utility is left for one skilled in the art and practicing the invention to discover.

In the present instance, the specification fails both to demonstrate the presence of a single identified peptide that meets a test requirement using the method claimed. The specification does not provide any guidance as to how one may screen for a test requirement. Accordingly, the total lack of specification regarding what test requirements are to be met, how to assess whether a test requirement is met, what indicia to measure, or activity the indicia are for necessarily places undue experimentation on the public to determine how to use this invention.

The specification and claims also fail to provide essential steps that are required to practice the claimed invention and require undue experimentation in order use the claimed invention. For example, measuring the indicia of an activity without any direction as to the activity to screen for does not enable one of skill in the art to use the invention because the activity, indicia of activity, and experimental conditions are left for the practitioner to determine. Experimentation required would include determination of chemical components, cells, and/or organisms to be included, identities and concentrations of peptides, temperature, pH, duration of the experiment and other parameters required to test for indicia. Similarly, determining a relationship between the measured first indicia of the activity and at least one whole molecule parameter of the plurality of first test peptides leaves it up to the practitioner of the invention to

discover a relationship and a method for expressing such a relationship. The means of determining a test requirement relating to the measured first indicia and identifying a second test peptide library containing a plurality of second test peptides which, based on the relationship, are expected to provide second indicia of the activity that meats the test requirement are also left to the practitioner of the invention.

The specification sites "operations" to be performed by one using the claimed invention. Page 7, lines 11-14 state that the test requirement may be determined before or after "operations" to determine a relationship between parameters and indicia. "Operations are also performed to identify a second test library" is sited on page 7, line 27. The operations referred to in the specification would require undue experimentation because they depend upon knowledge that must ultimately be obtained through experimentation. The specification provides lists of methods to be used to determine relationships between measured indicia and whole molecule parameters and other steps of the invention. These lists rather than providing guidance, however, simply summarize the current state in the art.

35 U.S.C. 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. **Claims 74-95 are rejected under 35 U.S.C. 112, first paragraph.** Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

2. **Claim 74-78, 80-82 and claims dependent thereon are rejected under 35 U.S.C. 112,** first paragraph, because the specification, while being enabling for short peptides (i.e. < 20 amino acids) for which the activity, indicia of activity, method of testing indicia, and relationship between indicia and whole molecule parameters are already well established, does not reasonably provide enablement for longer peptides or peptides for which structure-function relationships for specific activities, indicia, and peptides are not already well established. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Additionally, Claim 74 and claims dependent thereon are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Method steps describe determining and measuring first indicia of an activity, determining a relationship between measured first indicia of the activity and at least one whole molecule parameter, determining a test requirement relating to the measured first indicia, and identifying a second test peptide library are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Claim 74 recites a method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement. This encompasses **any** peptide, indicia, activity, and test requirement, the combinations of which are essentially limitless. The method steps of the claim recite determining a relationship between measured first indicia and at least one whole molecule

parameter of first test peptides, determining a test requirement, and identifying a second test peptide library. Although there are numerous ways of determining relationships between indicia and parameters, the methods do not provide means for determining any relationship or necessarily a relationship that will enable the successful use of the invention. Determining structure function relationships also require that the indicia of activity and activity be known. For this reason, essential method steps that are required for using the claimed invention are missing. The missing required method steps include the means of selecting a test peptide library, measuring indicia, determining test requirements, selecting and applying methods of determining relationships between indicia of activity and whole molecule parameters, determining test requirements, and selecting second test peptide libraries.

While methods similar to the claimed invention have met with limited success using well characterized peptides and well established structure-function relationships, these results cannot be extrapolated to encompass all peptide libraries, activities, indicia, whole molecule parameters, and structure-function relationships. See Norinder, Ulf, Peptides, 12:1223-1227, discussion, third paragraph and Zheng et al. J. Chem. Inf. Comput. Sci., 38:251-258, conclusion. These references indicate that the success of using structure-function relationships to identify second test compound libraries, including peptide libraries, depends on having well characterized lead compounds and relatively small peptides. Potential success is also dependent upon the methods of determining structure function relationships. See Hellberg et al., J. Med. Chem. 30: 1126-1135, last paragraph 1128-1129. The current state of the art, based upon the references sited, does not enable the scope of claim 74 which includes virtually infinite numbers of peptide libraries and activities and only vague guidance as to the methods to be used for determining relationships between whole molecule parameters and measured indicia (i.e. structure-function relationships).

The specification refers to "operations" to be performed on page 7, lines 12 and 27, indicating that additional steps are required to use the invention. In order to use the invention, one is required to measure an indicia of a plurality of test peptides. Without additional method steps, one of ordinary skill in the art would be required to experiment in order to determine test requirements, indicia and means of measuring them. On page 8, lines 15-20 of the specification, applicant lists methods that can be used to determine relationships between parameters and indicia of the measured property. There are numerous potential methods for determining structure function relationships in addition to those listed in the specification. Whether the method will ultimately lead to the successful use of the claimed invention depends upon the method selected, peptide library, indicia, activity, and the availability of data for determining the relationship. Listing potential methods without indicating any correlation between these methods and how they are to be applied or to what indicia, activity, or library they are to be applied, does not enable one of ordinary skill in the art to use the claimed invention. These lists rather than providing guidance, however, simply summarize the current state in the art.

With regard to **Claims 75-78,** the specification does not provide a means of applying a space-filling technique to test peptide libraries (Claim 75). Page 10, lines 16, lists exemplary space-filling designs but the specification does not provide direction for one skilled in the art on what design to use or how to apply a particular space-filling design to test peptide libraries. Claim 76 provides a general equation that relates a test parameter to an estimate of the first indicia of the activity of the plurality of first test peptides. The specification does not provide a means of measuring or estimating the first indicia of the activity of the plurality of first test peptides. With regard to Claim 77, the specification does not describe how to determine a range of acceptable indicia of the activity. For Claim 78, the specification does not describe how the

plurality of second test peptides can be determined from the estimated indicia that are within the range of acceptable indicia.

With regard to **Claims 80-82,** the specification does not describe a means of determining a distance function between a first value of a whole molecule parameter of a first test peptide and a second whole molecule parameter of a second test peptide not within the first test peptide library for Claim 80. The specification also fails to describe a means of estimating indicia of the activity of the second test peptide or how and in what instances a cutoff distance is to be determined and used. Nor does the specification does not describe how a first test peptide library of Claim 81 is defined or what constitutes a "candidate peptide." There is no algorithm disclosed that allows one to determine which peptides to use, how many, or which groups of peptide isomers to use as a candidate peptide. The specification does not describe how or under what circumstances one expands less than all of the candidate peptides determined in the representing step into their constituent compound peptides using a space filling technique for Claim 82.

35 U.S.C. 112 Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. **Claims 74-82, 85, 94, 95 and claims dependent thereon are rejected under 35 U.S.C. 112, second paragraph,** as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 74 is "a method of identifying a peptide with a predicted indicia of an activity that satisfies a test requirement" but the final step of the method is "identifying a second test peptide library containing a plurality of second test peptides which based on the relationship are expected to provide second indicia of the activity that meets the test requirement." It is not clear whether applicant intends the method to identify a single peptide in the first test peptide library, a single peptide in the second test peptide library, or a second test peptide library.

Claims 74, 77, 78, 80, 91 and claims dependent thereon: The phrase "indicia of an activity" is vague and indefinite in the context recited because the metes and bounds of the patent protection desired are unascertainable. The phrase is neither defined in the specification nor would it be apparent to one of ordinary skill in the art. It is not clear if there is a difference between "activity" and "indicia of an activity."

Claim 75 and claims dependent thereon: It is not clear from the specification or the claim what means of selection constitutes a space-filling technique for determining infringement. The claim is unclear as to applicants intent.

Claim 76 and claims dependent thereon: This claim includes the term "parameter" and "whole molecule parameter." It is not clear whether these terms are interchangeable or, if they are not interchangeable, how their meanings differ from one another.

Claims 77, 78, and claims dependent thereon: The term "acceptable" in claim 77 is a relative term which renders the claim indefinite. The term "acceptable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one

of ordinary skill in the art would not be reasonably apprised of the scope of the invention. One of ordinary skill in the art would not know how to determine whether an "indicia of the activity" is "acceptable" or not.

Claim 79 and claims dependent thereon: It is not clear from the claim or specification what the metes and bounds are for a "non-parametric regression formula," are or how one of ordinary skill in the art would ascertain whether the relationship determined in claim 76 is encompassed by the term "non-parametric regression formula."

Claim 81 and claims dependent thereon: The term "candidate peptide" in claim 81 is a relative term which renders the claim indefinite. The term "candidate peptide" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not possible to ascertain the metes and bounds of what constitutes a "candidate peptide."

Claim 81 and claims dependent thereon: While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). The term "peptide isomers" in claim 81 is used by the claim to mean peptides "sharing common global characteristics," while the art accepted meaning is peptides "sharing the same formula but having different properties" (Zumdahl, Steven S., "Chemistry", 4th ed., Houghton Mifflin Company, 1997). On page 48 of the specification, lines 7-12, applicant defines "compound isomers" as "the group of compounds sharing common global characteristics" and gives two examples of how the term may apply to peptides. Despite two examples of how the term ***can be*** applied to peptides, peptides are compounds and the term "peptide isomers" is therefore defined in the

specification as peptides "sharing common global characteristics." This definition is repugnant to the usual meaning of that term.

Claim 82 and claims dependent thereon: The term "compound peptide" has no generally accepted meaning and is not defined in the specification. It is not clear if there is a difference between a "peptide" and a "compound peptide."

Claim 85 and claims dependent thereon: Claim 74, upon which claim 85 depends, refers to "whole molecule parameter" while claim 85 refers to "parameter." It is not clear whether the terms are interchangeable. Therefor there is insufficient antecedent basis for this limitation in the claim.

Claims 94 and 95: The terms "about twenty," "about ten, "and "about four" in claims 94 and 95 are relative terms which render the claims indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not possible to ascertain how many more or fewer than 20 or 10 amino acids constitutes "about twenty" or "about ten" amino acids. Similarly, it is not possible to ascertain how many more or fewer than 4 amino acids constitutes "about four" amino acids.

Claim 94: Claim 94 is dependent on claim 74 which refers a first test peptide library and a second test peptide library. Claim 94 limits claim 74 by stating "wherein the test peptide library consists of peptides having a length in a range from about four to about twenty amino acids." It is not clear whether claim 94 limits the first test peptide library, the second test peptide library, or both test peptide libraries.

Claim 95: Claim 95 is dependent on claim 74 which refers a first test peptide library and a second test peptide library. Claim 95 limits claim 74 by stating "wherein the test peptide library consists of peptides having a length in a range from about four to about ten amino acids." It is not clear whether claim 94 limits the first test peptide library, the second test peptide library, or both test peptide libraries.

35 U.S.C. 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. **Claims 74, 81, 87- 90, 94, 95 are rejected under 35 U.S.C. 102(b)** as being anticipated by Tenson et al., The Journal of Biological Chemistry, 272:17425-17430, 1997 (Tenson et al.).

Claim 74: Tenson et al. anticipates each of the method steps of claim 74 (page 17427, left column). The ability of bacterial colonies to grow erythromycin containing agar plates reads on the claimed indicia of an activity of a plurality of first test peptides. Peptide length reads on the claimed relationship between measured indicia and whole molecule parameter. The ability of colonies to grow on erythromycin containing culture media plates reads on the claimed determining a test requirement relating to the measured first indicia. A second test peptide library containing pentapeptides reads on the claimed identifying a second test peptide library based on the relationship between peptide length and the ability to confer erythromycin resistance.

Claim 81: Tenson et al. anticipates defining a first test peptide library by representing each of a plurality of groups of peptide isomers from a first peptide space as a representative candidate peptide. By not expressing and screening all possible 21-mer peptides, Tenson et al. reads on the claimed defining a first test peptide library by representing each of a plurality of groups of peptide isomers from a first peptide space as a representative candidate peptide. Approximately 10^5 different 21-mer peptides were screened whereas the total number of possible 21-mer peptides is far greater. See page 17427, first paragraph of the reference.

Claim 87: Tenson et al. anticipates claim 87 because conferring erythromycin resistance reads on the claimed activity is binding to a receptor. The mechanism by which the peptides used by Tenson et al. confer erythromycin resistance is their ability to bind to the ribosome which is a receptor for elongation and termination factors and other regulatory molecules.

Claim 88: Tenson et al. anticipates claim 88 because the ability to grow in the presence of erythromycin reads on the claimed enhancement or inducement of a biological activity in a cell.

Claim 89: Tenson et al. anticipates claim 89 because inhibiting cell lysis in the presence of erythromycin reads on the claimed inhibition or prevention of a biological activity.

Claim 90: Tenson et al. anticipates claim 90 because the E.coli cultured in vitro reads on the claimed cell cultured in vitro.

Claim 94: Tenson et al. anticipates claim 94 because the 21 and 5 amino acid length peptides read on the claimed range from about four to about twenty amino acids.

Claims 95: Tenson et al. anticipates claim 95 because the 21 and 5 amino acid length peptides read on the claimed range from about four to about ten amino acids.

2. **Claims 74, 92, 94, 95 are rejected under 35 U.S.C. 102(b)** as being anticipated by Ostrem et al, Biochemistry 37:1053-1059 (1998).

Claim 74: Each of the method steps of claim 74 are anticipated by Ostrem at al. The ability of test peptides to bind to factor Xa reads on the claimed measuring indicia of an activity of a plurality of first test peptides (page 1054 first paragraph and page 1055 second paragraph). Determining a peptide length of 8 amino acids reads on the claimed determining a relationship between the measured first indicia of the activity and at least one whole molecule parameter of the plurality of first test peptides (page 1053, last paragraph). An assay of factor Xa activity reads on the claimed determining a test requirement relating to the first measured indicia (page 1054, first paragraph). Identifying a subset of the first peptide library and, based upon their ability to bind factor Xa, using the peptides in a prothrombinase assay reads on the claimed identifying a second test peptide library (page 1055, table 1 and figure 1). The authors also synthesized derivitized peptides and assayed them in coaagulation assays (figure 5, page 1057).

Claim 92: Ostrem et al. anticipates this claim because factor Xa acts both as a protease and as a receptor for factor Va and so reads on the claimed activity is inhibition or prevention of activation of a receptor (page 1053, first paragraph).

Claims 94: Ostrem et al. anticipates using octamers which reads on the claimed range of from about four to about twenty amino acids.

Claims 95: Ostrem et al. anticipates using octamers which reads on the claimed range of from about four to about ten amino acids.

3. **Claim 74 is rejected under 35 U.S.C. 102(b)** as being anticipated by Cho et al J. Chem. Inf. Comput. Sci., 38:259-268 (1998).

Each of the method steps of claim 74 are anticipated by Cho at al. The ability to potentiate bradykinin activity reads on the claimed measuring indicia of an activity of a plurality of first test peptides (page 261, right column, second paragraph). Twenty-eight peptides were used to generate QSAR equations which reads on the claimed determining a relationship between indicia of activity and at least one whole molecule parameter. Amino acid sequence similarity to known bradykining potentiating peptides reads on the claimed determining a test requirement relating to the measured first indicia. The peptide library including two peptides with higher activity than those included in the first test peptide library reads on the claimed identifying a second test peptide library. These peptides were identified based on the relationship between first measured indicia and the relationship determined between first indicia and at least one whole molecule parameter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Thomas W. Prasthofer** whose telephone number is **(703) 308-4548**. The examiner can normally be reached on Monday-Friday, 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

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12/15/00

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